

Version With Markings to Show Changes Made

REPLACEMENT PAGE 14

Gamborotta et al teaches a classic competitive inhibitor wherein the oligomers have sequence homology to *transcriptional [factors] factor-binding DNA sequence elements*, and, at high concentration of inhibitor, saturation binding of the transcriptional factors occurs, and maximum inhibitory effect is seen through inhibition of transcription alone. See Gamborotta, et al., p. 1914, Fig. 6. The present invention requires that muting occur at both the transcriptional and post-transcriptional levels. That is mechanistically impossible for the inhibitor oligomers of Gamborotta et al, and those skilled in the art would understand the clear difference between the Gamborotta reference and the presently claimed invention.

There is another major difference between the mechanism of action featured by the Gamborotta example and the transcriptional effect of the current invention: The oligonucleotides used in Gamborotta's work essentially titrate out a particular transcriptional factor in order to see a maximal transcriptional inhibition. Such performance is intrinsically non-specific to the inhibition of a particular gene expression, as experienced and mentioned in Gamborotta publication. By contrast, the transcriptional inhibition featured by identified muting fragments is not quantitative and is gene-specific. In other words, adding more of the same fragments does not necessarily increase the level of gene suppression. Applicants believe, the way that transcriptional component of muting works is, due to the fact that each identified muting DNA fragment carries several regulatory sequence elements, the overall local disturbance of the transcriptional complex caused by the presence of the muting DNA in the nucleus results in specific transcription shut down of the endogenous gene.

In conclusion, for the reasons stated above, it is respectfully submitted that all pending claims are in condition for allowance. Reconsideration of the claims, consideration of the added claims, and a notice of allowance is therefore requested.

It is believed that a one-month extension of time is needed; however, this conditional petition for an extension of additional time is being made in the event that the need for more than a one-month extension has been overlooked. Please charge deposit account number 19-4972 for the one-month extension fee. If any additional fees are required for the timely consideration of this application, please charge deposit account number 19-4972. The Examiner is requested to telephone the undersigned if any matters remain outstanding so that they may be resolved expeditiously.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment, captioned "Version With Markings to Show Changes Made."